

### **ABSTRACT**

Compositions and methods for selectively killing a cell containing a viral protease are disclosed. The composition is a variant of a protein synthesis inactivating toxin wherein a viral protease cleavage site is interposed between the A and B chains. The variant of the type II ribosome-inactivating protein is activated by digestion of the viral protease cleavage site by the specific viral protease. The activated ribosome-inactivating protein then kills the cell by inactivating cellular ribosomes. A preferred embodiment of the invention is specific for human immunodeficiency virus (HIV) and uses ricin as the ribosome-inactivating protein. In another preferred embodiment of the invention, the variant of the ribosome-inactivating protein is modified by attachment of one or more hydrophobic agents. The hydrophobic agent facilitates entry of the variant of the ribosome-inactivating protein into cells and can lead to incorporation of the ribosome-inactivating protein into viral particles. Still another preferred embodiment of the invention includes a targeting moiety attached to the variants of the ribosome-inactivating protein to target the agent to HIV infectable cells.